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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,957	06/18/2001	Rose Ramon Botella Mesa	DAVI199.000GEN	3466

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	09/763,957	BOTELLA MESA ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2008 and 03 July 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 7, 9, 11-15, 19-24 and 26-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,9,11-15,19-21,38 and 39* is/are rejected.

7)☒ Claim(s) *26-35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/24/09 has been entered. Claims 1, 7, 9, 11-15, 19-21 and 26-39 are pending.

Claim Objections

In claim 7, the recitation, "a primer corresponding to all or part of SEQ ID NO:1 or a complementary for thereof and cloning DNA upstream of the region of the primer, wherein the promoter comprises any one of:" lacks clarity. 1) as added to the rejection below, the recitation of a pat of SEQ ID NO:1 as a primer complicates the method as such a recitation is not size limited and therefore can encompass portions that are so small that they will bind non-specifically. 2) The step of "cloning DNA upstream of the region of primer hybridization" also lacks adequate size limitation but also does not indicate into what the DNA is inserted. It would be remedial to amend the phrase to recite, -- a primer corresponding SEQ ID NO:1 or a complementary for thereof and isolating nucleic acid upstream of the primer that comprises any one of: --. This last amendment is recommended for step (iv) of claim 9.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

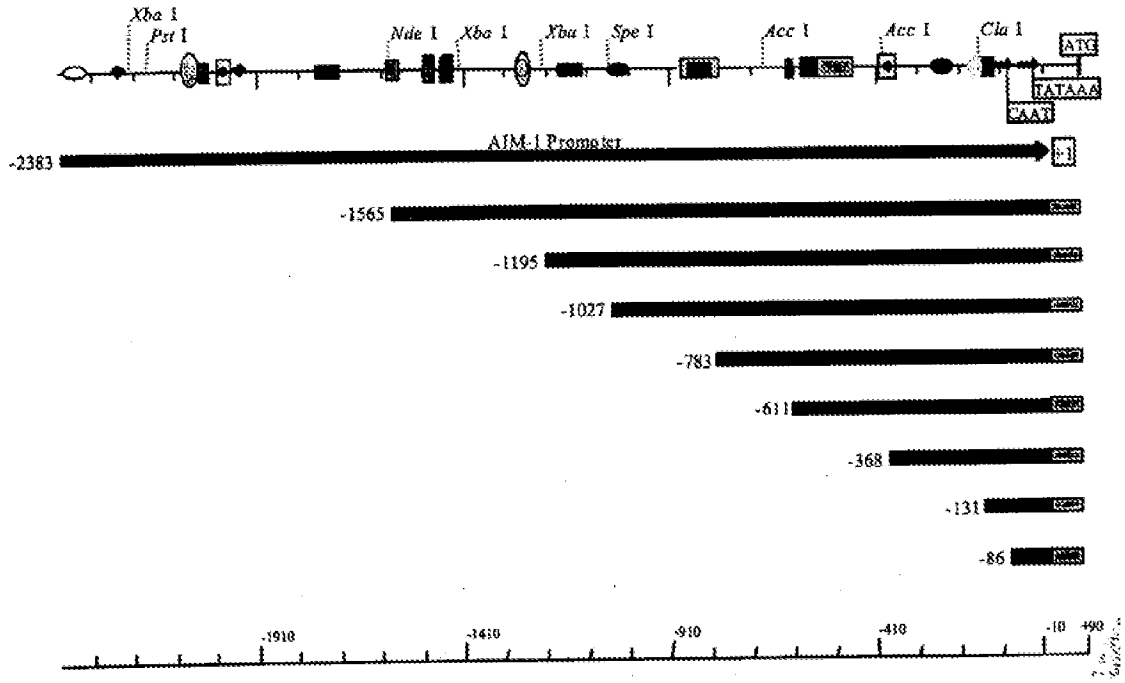
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment.**

The limitation that the promoter comprises a fragment comprising residues 2298-2384 has been added by newly added claim 38 and 39.

FIGURE 12



Applicants' amendment to recite that the claimed promoter comprises sequences 2384-2473 is not supported by the text. These sequences are said to be the grayed region in figure 12. Applicants' have isolated the promoter region of AAC-1 synthase which is disclosed as SEQ ID NO:3. SEQ ID NO:3 is 2474 nucleotides. In the arguments filed 12/6/06, applicants have described the components of this figure. "The line at the foot of Figure 12 indicates that the ATG ends at nucleotide +90. The ATG at the end of SEQ ID NO: 3 is at nucleotides 2471 to

2473. Accordingly, nucleotides 2471 to 2473 of SEQ ID NO: 3 are nucleotides 88 to 90 of Figure 12. Thus, the sign "+1" of Figure 12 referred to in the claims is nucleotide 2384 of SEQ ID NO: 3.". The promoter is therefore, found in nucleotides 1 to 2384 of SEQ ID NO:3. Hence, by applicants' arguments, these sequences are not part of the promoter region. Secondly, the "promoter" region is further defined by serial deletions of the sequences to 2298 of SEQ ID NO:3 (-86 above). The results indicate in figure 11 that fragments of the promoter were tested are not inclusive of 2384-2473. While this region exists in the claims, neither the figures nor the disclosure teach that this region is contemplated as a fragment of the ACC-1 promoter. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." Lockwood v. American Airlines Inc., 41 USPQ2d 1961, 1966 (CAFC 1997). Therefore, the limitation is impermissible NEW MATTER.

Claims 1, 7, 9, 11-15 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid sequence defining a promoter wherein the sequence is SEQ ID NO:3 or a fragment comprising nucleotides 2016-2384, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **This**

rejection is maintained for reasons of record in the office action mailed 6/6/06 and 3/26/07 and . The rejection has been slightly reworded based upon applicants' amendment.

1) Nature of invention. The invention is drawn to an isolated sequence that defines a promoter. The specification teaches that the operative goal of the invention is to provide a promoter that directs expression of a gene encoding ACC synthase and is inducible in response to physical stimulation.

2) Scope of the invention. To this end, applicants claim a genus of sequences that are nucleotide sequences that "define a promoter". Specifically, this genus comprises multiple sequences 1) a sequence of nucleotides having the sequence as set forth in SEQ ID NO:3, 2) a fragment comprising residues 2298 to 2384, 3) nucleotides with at least 95% identity to residues 2298-2384 of SEQ ID NO:3, 4) a sequence of nucleotides complementary to these sequences. Applicants recite a broad genus of sequences that appear to be functionally defined by being capable in their native form to direct expression of a gene encoding ACC synthase and that is further inducible. While it is presumed that the fragment must be able to encode an inducible promoter that can direct expression of a gene encoding ACC synthase, the specification does not provide adequate description in the specification of the required structural aspects of the sequences to provide this function. The structural requirements are further confused by reciting the sequences in terms of 95% identity. The result of this reaction need not comprise a promoter or promoter related sequences. For example, a sequence lacking sequences essential for promoter function can result in a nucleic acid sequence that is almost 100% related sequentially to regions of SEQ ID NO: 1 but has no relationship functionally. Furthermore, these sequences may or

may not provide functional characteristics that are commensurate in scope with the disclosed function of the vector.

3) Number of working examples and guidance. Functionally, applicants disclose that sequences that "define a promoter" "confers, activates or enhances expression of a structural gene or other nucleic acid in a plant cell" (see page 16, paragraph 5). Structurally, applicants disclose the sequence of pGEL-1 (SEQ ID NO:3). pGEL-1 comprises the promoter from mung bean ACC synthase that directs expression of a protein encoded by a sequence with 100% identity to SEQ ID NO: 1. Primer pairs 4 and 5 are used to isolate the promoter from mung bean. To characterize the promoter, applicants generate a series of seven serial deletions of the mung bean ACC synthase promoter region (page 36). A general decline in activity in the shorter promoters is detected in immature and mature leaf tissue but not evidently in any other tissues (page 37).

4) State of the art. The art does not disclose SEQ ID NO:3. Nor does the art or the specification teach the acc synthase promoter from mung bean or domains/ motifs required for promoter activity by the acc synthase promoter. Therefore, as neither domains nor structural motifs are available, the ability to identify

5) Unpredictability of the art. Applicants claim an isolated nucleic acid molecule that defines a promoter. However, applicants only disclose a single sequence that meets these functional limitations and that is SEQ ID NO:3. Even the steps of claim 9, which are designed to isolate a promoter from native DNA will isolate a sequence corresponding to SEQ ID NO:3. By reciting sequences with 95% homology to residues 2298-2384 of SEQ ID NO:3 applicants claim sequences that can differ in any of 5% of the nucleotides of SEQ ID NO:3. This analysis

requires a clear understanding of the structural requirements of the promoter and what nucleotides are unalterable and which are not. By disclosing pGEL-1, the applicants have not reduced to practice the claimed invention. Applicants have not demonstrated a representative number of sequences that comprise relevant identifying characteristics, specific features or functional attributes that would distinguish different members of the claimed genus. In other words, a number of sequences fit into this broad genus of sequences that can potentially be isolated but the skilled artisan cannot envision the detailed structure of the broad class of sequences that are in their native form capable of directing expression of ACC synthase and are inducible given the lack of adequate description of structural requirements. Because applicants do not provide the structural requirements of the sequences of the fragment of SEQ ID NO:3 that "confers, activates or enhances expression of a structural gene or other nucleic acid in a plant cell", deviation from the entire sequence of nucleotides of pGEL-1 that can perform the same function are not known. Nor can the sequences that cannot be altered or cannot be deviated from cannot be guessed. Isolation of a promoter from such sequences requires a detailed understanding of the structural requirements of the promoter. Applicants' disclosure has amounted to a statement that the protein is part of the invention and a reference to a potential method for isolating it, by sequence identity. It would require undue experimentation to identify those molecules that are 95% identical to SEQ ID NO:3.

6) Amount of Experimentation Required. The specification provides a single reference sequences without identifying relevant characteristics or structural-functional relationships. Thus neither the specification nor the prior art teach the structural requirements of sequences with at least 95% similarity to a fragment comprising residues 2298-2384 of SEQ ID

NO:3 or a complement of these sequences. Given the large size and diversity of the recited sequences, the absence of disclosed or art recognized correlations between structure and function and the large number of potential sequences or homologs, it must be considered that any sequence with promoter activity in a plant cell must be empirically determined.

Response to Argument

Applicants' arguments filed 7/3/08 have been fully considered but they are not persuasive. The guidance provided by applicant in the as-filed application does not demonstrate an understanding of the structural requirements that are required for such promoter function except to teach SEQ ID NO:3 and demonstrate that the promoter has a general decline in activity as the sequence is serially deleted in immature and mature leaf tissue but not evidently in any other tissues (page 37). Applicants claim all nucleic acid sequences that are related by at least 95%. However, such claims are rejected under 35 USC 112, first paragraph for lack of enablement. The claims have been amended to be drawn to a fragment that is related to the smallest fragments of the promoter assayed. While the fragment from 2298-2384 is only 86 nucleotides and detection of a sequence that is 95% related should allow for less alteration than in larger fragments, the amendment does not overcome the basis of the rejection. First, the claims are drawn to "a fragment of (i), wherein said fragment comprises residues 2298-2384." Therefore, the fragment is not size limited and therefore and can comprise the entirety of SEQ ID NO:3. Secondly, in the absence of their structural requirements, the relationship between the structure of the sequence and its function becomes unclear. Thus a person of ordinary skill in the art could not predict the operability of the species that are 95% related. The inherent properties

of SEQ ID NO:3 that are responsible for expression are unknown as neither the specification nor the art characterize these sequences such that a cause and effect of mutations of the sequences are known. Hence, it is not clear how the instant promoter distinguishes itself from art available inducible promoters.

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim absent the structural requirements. In re Soil, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; In re Wahlforss, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. In this case, it is not clear that SEQ ID NO:3 absent identifiable structural and functional requirements can be used to identify the genus of recited fragments. Where a claim purports to cover all nucleic acids that encode a specific protein and the specification discloses but a single DNA known to do so, the situation is analogous to a single means claim and does not meet the enablement requirement under para. 1 ' of§112. The guidance in the specification does not detail the sequences of the promoter that can be altered. Furthermore, the ability to determine a priori whether a homologue or variant can function in the recited invention is not a high art. A particular sequence determines its structural, and functional properties, and a predictability of a representative number of claimed sequences that display noteworthy biological properties

requires a knowledge of and guidance with regard to which sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which a structure relates to its functional usefulness. Specifically, Lesk et al teach that methods that have been applied to function prediction work only part time and only function to predict potential function. As the structural requirements of the promoters are unknown, the ability to identify sequences with at least 95% sequence identity presents a lack of operability in that it is not known what nucleic acids must and what must not be mutated. What is required is an understanding of the required promoter sequences but as applicants do not demonstrate those sequences required for this function, and coupled with the ability to determine a priori which amino acids are required; there is considerable unpredictability to the claimed invention. To identify these sequences at this point would be an inventive step that is not supported by the guidance in the specification. In other words, the specification does not provide the teachings that would lead one to those regions or nucleotides that are critical within these fragments. Hence the structural requirements of the desired promoters are vitually unknown and undue experimentation would be required to assess the potentially functionally diverse population of seqeunces with 95% homology.

Conclusion

Claims 1, 7, 9, 11-15, 19-21, 38 and 39 are rejected.

Claims 26-35 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich/
Primary Examiner, Art Unit 1633